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| 10/742,346 | 12/19/2003 | Robert Falotico | CRD-5062 USANP | 6421 |

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| EXAMINER | |
|---|---|
| HELM, CARALYNNE E | |
| ART UNIT | PAPER NUMBER |
| 1615 | |

| NOTIFICATION DATE | DELIVERY MODE |
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| 07/21/2011 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/742,346 | FALOTICO ET AL. | |
| | Examiner | Art Unit | |
| | CARALYNNE HELM | 1615 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *31 May 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *6-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 31, 2011 has been entered.

### *Election/Restrictions*

To summarize the current election, applicants elected group I, without traverse.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. It is not clear from the original disclosure that

applicants envisioned a basecoat layer and topcoat layer applied such that the two layers do not blend. A review of the disclosure has not uncovered written or implicit basis and applicants have neither pointed to particular citations nor provided any explanation of how the new limitation has basis in the original disclosure.

This is a new matter rejection.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The four factual inquiries of Graham v. John Deere Co. have been fully considered and analyzed in the rejections that follow.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6 and 7 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Hossainy et al. (US Patent No. 7,285,304) in view of Hossainy et al. (US Patent No. 6,153,252 - henceforth Hossainy B) and Tseng et al. (previously cited).

Hossainy et al. teach a stent (implantable structure) that is coated with a basecoat of poly(vinylidene fluoride-co-hexafluoro propene) (also known as poly(vinylidenefluoride-co-hexafluoropropylene)) (PVDF-HFP) that includes a rapamycin analog (see example 5; instant claims 6 and 7). This polymer meets the limitation of a fluoropolymer in the first material. Applicants recite in the specification that rapamycin and its analogs are included in the recitation of "rapamycin"; therefore the recited analog in the example of Hossainy et al. meets the limitation for rapamycin (see paragraph 101). Additionally, rapamycin is also taught as the drug in the reservoir layer (see column 19 lines 4-6). Hossainy et al. teach a topcoat layer on top of such a drug reservoir layer to slow the rate of release of the drug (see column 4 lines 12-24). Coatings composed of poly(n-butyl methacrylate) (PBMA) are taught as especially suitable as this topcoat layer (see column 21 lines 11-12; instant claim 6). This polymer meets the limitation of an acrylate in the second material and is immiscible with PVDF-HFP. A diagram of these coating layers shows them as separate and distinct layers

(see figure 1D; instant claim 6). Hossainy et al. do not explicitly teach the presence of trichostatin A, the amount of PBMA in the topcoat layer, or that the topcoat and basecoat do not blend.

Hossainy B teaches the preparation of a stent with both a drug reservoir (basecoat) layer and a topcoat that slows the rate of release of the drug (see abstract and column 7 lines 18-21). The topcoat is taught to be a polymer that is present at 300 to 1600 μg (column 7 lines 23-34; instant claim 6). Hossainy B further teaches the application of a topcoat polymer in a solvent that does not solubilize the underlying drug layer (see column 7 lines 34-40). Such an application does not allow the two layers to blend.

Tseng et al. teach a stent (an implantable structure), containing drug depots capable of controllably delivering one or more histone deacetylase (HDAC) inhibitors which inhibit smooth muscle cell proliferation (see paragraph 37; instant claims 6-7). Specifically, the HDAC inhibitor depot is envisioned as a coating on the stent (see paragraph 118; instant claim 6). In addition, Tseng et al. also teach that the disclosed device delivering the HDAC inhibitors is particularly beneficial in the treatment of restenosis, implying that the HDAC inhibitors would be present at therapeutic dosages within the stent device (see paragraph 37; instant claim 6). Tseng et al. go on to further describe the HDAC inhibitor included on or in the stent body as trichostatin A, abbreviated as TSA (see claims 12-14 and paragraph 15 lines 1-2; instant claim 9). Tseng et al. teach the effectiveness of TSA at 50 nano molar on the inhibition of smooth muscle cell proliferation (see paragraph 168; instant claim 6). Also taught by Tseng et

al. is the inclusion of an additional pharmaceutical agent or agents, such as anti-inflammatory and anti-proliferative agents, where an exemplary agent includes rapamycin as a preferred option (see paragraph 134 and claims 2 and 3; instant claim 6).

It would have been obvious to one of ordinary skill in the art at the time of the invention to apply a topcoat composed of PBMA on the stent of example 5 in Hossainy et al. from a solvent that does not solubilize the PVDF-HFP and at 300 to 1600 μg as taught by Hossainy B. This modification would have been obvious as the application of the same technique to a similar device to improve it in the same way. Additionally, it would have been obvious to include TSA in the basecoat layer along with rapamycin or its analog, given the teachings of Tseng et al. to couple these compounds in a drug delivery depot on a stent. The inclusion of this compound at 50 nano molar as taught by Tseng et al. then flows naturally from these teachings. In addition, the term "affixed" is interpreted as “applied to” or “in contact with” based upon the description in the instant disclosure of how a coating or therapeutic becomes “affixed” to the device surface. Thus, the basecoat layer and topcoat layer of Hossainy et al. in view of Hossainy B and Tseng et al. are affixed upon each other and both TCA and rapamycin (or its analog) are releasably affixed to this device since the polymer provides for their controlled release.

Applicants teach that the presence of rapamycin (sirolimus) with TSA may potentiate each other’s anti-restenotic activity (see instant specification page 9 lines 21-25). According to MPEP 2112.01, “A chemical composition and its properties are

inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present." This treatment results from In re Spada, which states that, "Products of identical chemical composition can not have mutually exclusive properties." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Since Hossainy et al. in view of Hossainy B and Tseng et al. make obvious the claimed device with trichostatin A and rapamycin present in combination, it also would have the claimed potentiation effect between the two actives. Therefore claims 6 and 7 are obvious over Hossainy et al. in view of Hossainy B and Tseng et al.

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hossainy et al. in view of Hossainy B and Tseng et al. as applied to claims 6 and 7 above, and further in view of Carter et al. (previously cited).

Hossainy et al. in view of Hossainy B and Tseng et al. make obvious a stent with a basecoat layer that includes PVDF-HFP, TCA, and rapamycin as well as a topcoat layer composed of PBMA as recited in instant claim 6. The modified reference also teaches that the reason for incorporating the TCA within the stent device is for addressing the issue of restenosis following stent implantation (see Tseng et al. paragraphs 29, 31, and 37). Hossainy et al. in view of Hossainy B and Tseng et al. do not specifically teach stent grafts containing the layered coatings with controllable release capabilities.

Carter et al. teach that stents are commonly used to clear obstructions and to repair damage to vascular tissue (see paragraph 39 lines 2-5). Carter et al. go on to teach that stent grafts are a common name for a modification of stents where a flexible covering is attached to the stent frame (see paragraph 39 lines 10-12) and that the implantation process for stents, as a whole, carries with it the risk of causing restenosis (see paragraph 50 line 9). Since stent grafts are a modification of stents and also subject to post-implantation restenosis, it would have been obvious to one skilled in the art at the time of the invention to further modify the invention of Hossainy et al. in view of Hossainy B and Tseng et al., by applying their layered polymer coating configuration containing trichostatin A at about 50 nano molar and rapamycin to a stent-graft device. Therefore, instant claim 8 is obvious over Hossainy et al. in view of Hossainy B, Tseng et al., and Carter et al.

## ***Response to Arguments***

Applicant's arguments with respect to claims 6-8 have been considered but are moot in view of the new ground(s) of rejection.

The previous rejections made under 35 USC 103(a) are hereby withdrawn in favor of the new grounds of rejection presented above.

## ***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Friday 9-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Caralynne Helm/
Examiner, Art Unit 1615

/Juliet C Switzer/
Primary Examiner, Art Unit 1634